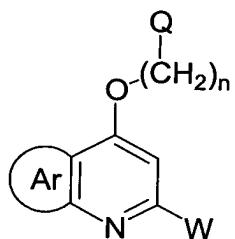
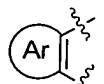


What is claimed is:

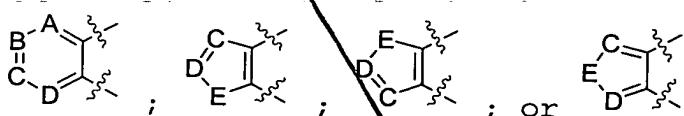
1. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:



5 represents:



wherein:

A, B, C, and D are independently nitrogen or CR₁, and
E represents oxygen, sulfur or NR₂,

10 wherein

when Ar is a 6-membered ring, 1 or 2 of A, B, C, and D are
nitrogen; and

when Ar is a 5-membered ring, C and D are both CR₁ and E
is nitrogen, sulfur, or NR₂,

15 where

R₁, at each occurrence, is independently selected
from the group consisting of hydrogen, halogen,
cyano, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy,
C₁₋₆ alkyl, amino, mono and di(C₁₋₆)alkylamino,
20 and C₁₋₆ alkoxy; and

R₂ is selected from the group consisting of hydrogen,
halogen, cyano, halo(C_{1-C₆})alkyl, halo(C_{1-C₆})alkoxy, hydroxy, C₁₋₆ alkyl, amino, and mono
or di(C_{1-C₆})alkylamino;

25 W is selected from the group consisting of aryl, heteroaryl,
and heterocycloalkyl, each of which is unsubstituted or
substituted with one or more R₃; and

~~Q~~ is selected from the group consisting of aryl, heteroaryl, and heterocycloalkyl, wherein each is unsubstituted or substituted with one or more of R₄;

5 R₅ and R₄ at each occurrence are independently selected from the group consisting of hydrogen, halogen, hydroxy, -OR₆, -NO₂, -CN, -SO₂NH₂, -SO₂NHR₆, -SO₂N(R₆)₂, amino, -NHR₆, -N(R₆)₂, -N(R₆)CO(R₆), -N(R₆)CO₂(R₆), -CONH₂, -CONH(R₆), -CON(R₆)₂, -CO₂(R₆), -S(R₆), -SO(R₆), -SO₂(R₆), and R₇, wherein

10 R₆, at each occurrence, is independently selected from the group consisting of C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkenyl, and C₅₋₉ cycloalkynyl, each of which is unsubstituted or substituted with one or more substituents selected from the group consisting of hydroxy, oxo, halogen, amino, C₁₋₈ alkoxy, and C₁₋₈ alkyl,

15 R₇ at each occurrence is independently selected from the group consisting of C₁₋₈ alkyl, C₁₋₈ alkenyl, C₁₋₈ alkynyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkenyl, and C₅₋₉ cycloalkynyl, each of which is unsubstituted or substituted with one or more substituents selected from the group consisting of hydroxy, oxo, halogen, -OR₆, C₁₋₆alkyl, -NO₂, -CN, -SO₂NH₂, -SO₂NHR₆, -SO₂N(R₆)₂, amino, -NHR₆, -N(R₆)₂, -N(R₆)CO(R₆), -N(R₆)CO₂(R₆), -CONH₂, -CONH(R₆), -CON(R₆)₂, -CO₂H, -CO₂(R₆), -S(R₆), -SO(R₆), -SO₂(R₆), and NR_aR_b, wherein each NR_aR_b independently forms a monocyclic or bicyclic ring each of which may contain one or more double bonds, or one or more of oxo, O, S, SO, SO₂, NH, or N(R₂), wherein R₂ is defined above and independently selected at each occurrence; or

30 35 Q is a group of the formula NR₈R₉ wherein

*Sub A2
CONT.*

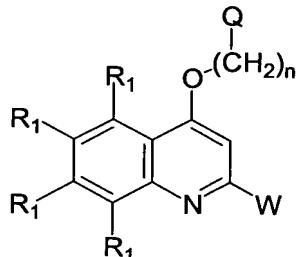
0 9 8 9 2 0 2 4 * 0 9 8 2 6 0 0 1

*Sub
A2
cont.*

~~R₈ and R₉ are independently hydrogen or R₇; or R₈, R₉ and the nitrogen to which they are attached form a heterocycloalkyl ring having from 5 to 8 ring atoms and where 1 or 2 of the ring atoms are selected from N, S, and Q, with remaining ring members being carbon, CH, or CH₂, which heteroacyclicloalkyl ring is unsubstituted or substituted with one or more independently selected R₄ groups; and~~

X is -(CH₂)_n- or -(CH₂)_n(C=O)-, wherein each n is independently 10 1, 2, or 3.

2. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:
each R₁ represents hydrogen, halogen, cyano, halo(C₁₋₆)alkyl,
halo(C₁₋₆)alkoxy, hydroxy, C₁₋₆ alkyl, amino, mono and
di(C₁₋₆)alkylamino, and C₁₋₆ alkoxy;

W is selected from the group consisting of aryl, heteroaryl,
and heterocycloalkyl, each of which is unsubstituted or
substituted with one or more of R₃;

Q is selected from the group consisting of aryl, heteroaryl,
and heterocycloalkyl, each of which is unsubstituted or
substituted with one or more of R₄; or

R₃ and R₄ at each occurrence are independently selected
from hydrogen, halogen, hydroxy, -OR₆, -NO₂, -CN,
-SO₂NH₂, -SO₂NHR₆, -SO₂N(R₆)₂, amino, -NHR₂, -N(R₆)₂,
-N(R₆)CO(R₆), -N(R₆)CO₂(R₆), -CONH₂, -CONH(R₆),
-CON(R₆)₂, -CO₂(R₆), -S(R₆), -SO(R₆), -SO₂(R₆), and R₇,
wherein

DRAFT - DRAFT - DRAFT

5 R₆, at each occurrence, is independently selected from the group consisting of C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkenyl, and C₅₋₉ cycloalkynyl, each of which is unsubstituted or substituted with one or more substituents selected from the group consisting of hydroxy, oxo, halogen, amino, C₁₋₈ alkoxy, and C₁₋₈ alkyl,

10 R₇ at each occurrence is independently selected from the group consisting of C₁₋₈ alkyl, C₁₋₈ alkenyl, C₁₋₈ alkynyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkenyl, and C₅₋₉ cycloalkynyl, each of which is unsubstituted or substituted with one or more substituents selected from the group consisting of hydroxy, oxo, halogen, C₁₋₆alkyl, -OR₆, -NO₂, -CN, -SO₂NH₂, -SO₂NHR₆, -SO₂N(R₆)₂, amino, -NHR₆, -N(R₆)₂, -N(R₆)CO(R₆), -N(R₆)CO₂(R₆), -CONH₆, -CONH(R₆), -CON(R₆)₂, -CO₂H, -CO₂(R₆), -S(R₆), -SO(R₆), -SO₂(R₆), and NR_aR_b, wherein each NR_aR_b independently forms a monocyclic or bicyclic ring, each of which may contain one or more double bonds, or one or more of oxo, O, S, SO, SO₂, NH, or N(R₆), wherein R₆ is defined above and independently selected at each occurrence; or

Q is a group of the formula NR₈R₉, wherein

30 R₈ and R₉ are independently hydrogen or R₇; or

35 R₈, R₉ and the nitrogen to which they are attached form a heterocycloalkyl ring having from 5 to 8 ring atoms and where 1 or 2 of the ring atoms are selected from N, S, and O, with remaining ring members being carbon, CH, or CH₂, which heterocycloalkyl ring is unsubstituted or substituted with one or more independently selected R₄ groups; and "

TOP SECRET//
REF ID: A65660

n is 1, 2, or 3.

3. A compound or salt according to claim 2, wherein:

n is 1.

5

4. A compound or salt according to claim 2 wherein W is phenyl or pyridyl, each of which is unsubstituted or substituted with 1 to 3 substituents independently selected from halogen, hydroxy, C₁₋₆alkoxy, -nitro, -CN, -SO₂NH₂, -SO₂NHR₂, -SO₂N(C₁₋₆alkyl)₂, amino, -NHC₁₋₆alkyl, -N(C₁₋₆alkyl)₂, -N(C₁₋₆alkyl)CO(C₁₋₆alkyl), -N(C₁₋₆alkyl)CO₂(C₁₋₆alkyl), -CONH₂, -CONH(C₁₋₆alkyl), -CON(C₁₋₆alkyl)₂, -CO₂(C₁₋₆alkyl), -S(C₁₋₆alkyl), -SO(C₁₋₆alkyl), -SO₂(C₁₋₆alkyl), and C₁₋₆alkyl optionally substituted with one or more substituents independently selected from hydroxy, halogen, and amino.

10 5. A compound or salt according to Claim 2 wherein

n is 1; and

W is phenyl or pyridyl, each of which is unsubstituted or substituted with 1 to 3 substituents independently selected from halogen, hydroxy, C₁₋₆alkoxy, -CN, amino, -NHC₁₋₆alkyl, -N(C₁₋₆alkyl)₂, and C₁₋₆alkyl optionally substituted with one or more substituents independently selected from hydroxy, halogen, and amino.

20 25

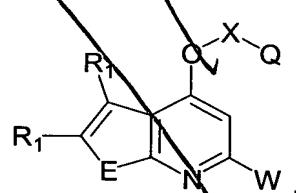
6. A compound or salt according to claims 2 wherein:

n is 1;

Q is selected from phenyl, pyridyl, pyrimidinyl, pyrazolyl, triazolyl, imidazolyl, pyrrolyl, piperidinyl, and 30 pyrrolidinyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C₁₋₆alkoxy, -CN, amino, mono- and di(C₁₋₆)alkylamino, and C₁₋₆ alkyl which is unsubstituted or substituted with 1 or more substituents

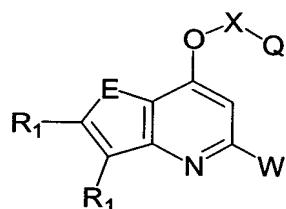
chosen from hydroxy, oxo, amino, halogen, C₁₋₆alkyl, and C₁₋₆alkoxy, and mono- and di(C₁₋₆)alkylamino; and
W is phenyl or pyridyl, each of which is unsubstituted or
substituted with from 1 to 3 substituents independently
selected from halogen, hydroxy, C₁₋₆alkoxy, -CN, amino,
-NHC₁₋₆alkyl, -N(C₁₋₆alkyl)₂, and C₁₋₆alkyl optionally
substituted with one or more substituents independently
selected from hydroxy, halogen, and amino.

10 7. A compound or salt according to claim 1 of the
formula:



15 8. A compound or salt according to claim 7, where E is
sulfur.

9. A compound or salt according to claim 1 of formula:



20 10. A compound or salt according to claim 9, wherein E is
sulfur.

25 Sub A3
11. A compound or salt according to Claim 10, wherein W
is phenyl or pyridyl, each of which is unsubstituted or
substituted with from 1 to 3 substituents independently
selected from halogen, hydroxy, C₁₋₆alkoxy, -nitro, -CN,
-SO₂NH₂, -SO₂NHR₂, -SO₂N(C₁₋₆alkyl)₂, amino, -NHC₁₋₆alkyl, -N(C₁₋

Sub
A³
con

ϵ alkyl)₂, -N(C₁₋₆alkyl)CO(C₁₋₆alkyl), -N(C₁₋₆alkyl)CO₂(C₁₋₆alkyl), -CONH₂, -CONH(C₁₋₆alkyl), -CON(C₁₋₆alkyl)₂, -CO₂(C₁₋₆alkyl), -S(C₁₋₆alkyl), -SO(C₁₋₆alkyl), -SO₂(C₁₋₆alkyl), and C₁₋₆alkyl optionally substituted with one or more substituents independently selected from hydroxy, halogen, and amino.

12. A compound or salt according to claim 9, wherein X is
CH₂.

10 13. A compound or salt according to claim 10, wherein X
is CH₂.

14. A compound or salt according to claim 13 wherein:

W is phenyl or pyridyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C₁₋₆alkoxy, -nitro, -CN, -SO₂NH₂, -SO₂NHR₂, -SO₂N(C₁₋₆alkyl)₂, amino, -NHC₁₋₆alkyl, -N(C₁₋₆alkyl)₂, -N(C₁₋₆alkyl)CO(C₁₋₆alkyl), -N(C₁₋₆alkyl)CO₂(C₁₋₆alkyl), -CONH₂, -CONH(C₁₋₆alkyl), -CON(C₁₋₆alkyl)₂, -CO₂(C₁₋₆alkyl), -S(C₁₋₆alkyl), -SO(C₁₋₆alkyl), -SO₂(C₁₋₆alkyl), and C₁₋₆alkyl optionally substituted with one or more substituents independently selected from hydroxy, halogen, and amino.

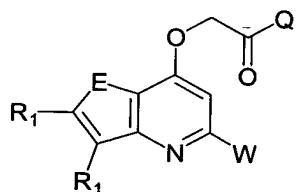
15. A compound or salt according to Claim 13; wherein Q is selected from phenyl, pyridyl, pyrimidinyl, pyrazolyl, triazolyl, imidazolyl, pyrrolyl, piperidinyl, and pyrrolidinyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C₁₋₆alkoxy, -CN, amino, mono- and di(C₁₋₆)alkylamino, and C₁₋₆ alkyl which is unsubstituted or substituted with 1 or more substituents independently chosen from hydroxy, exo, amino, halogen, C₁₋₆alkyl, C₁₋₆alkoxy, and mono- and di(C₁₋₆)alkylamino; and is phenyl or pyridyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently

*Sub
A4
5
cont.*

~~selected from: halogen, hydroxy, C₁₋₆alkoxy, -nitro, -CN, -SO₂NH₂, -SO₂NHR₂, -SO₂N(C₁₋₆alkyl)₂, amino, -NHC₁₋₆alkyl, -N(C₁₋₆alkyl)₂, -N(C₁₋₆alkyl)CO₂(C₁₋₆alkyl), -CONH₂, -CONH(C₁₋₆alkyl), -CON(C₁₋₆alkyl)₂, -CO₂(C₁₋₆alkyl), -S(C₁₋₆alkyl), -SO(C₁₋₆alkyl), -SO₂(C₁₋₆alkyl), and C₁₋₆alkyl which is unsubstituted or substituted with one or more substituents independently selected from hydroxy, halogen, and amino.~~

10

16. A compound or salt according to Claim 1 of formula:



~~17. A compound or salt according to Claim 16, wherein E is sulfur.~~

15

~~18. A compound or salt according to Claim 17, wherein W is phenyl or pyridyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C₁₋₆alkoxy, -nitro, -CN, -SO₂NH₂, -SO₂NHR₂, -SO₂N(C₁₋₆alkyl)₂, amino, -NHC₁₋₆alkyl, -N(C₁₋₆alkyl)₂, -N(C₁₋₆alkyl)CO₂(C₁₋₆alkyl), -CONH₂, -CONH(C₁₋₆alkyl), -CON(C₁₋₆alkyl)₂, -CO₂(C₁₋₆alkyl), -S(C₁₋₆alkyl), -SO(C₁₋₆alkyl), -SO₂(C₁₋₆alkyl), and C₁₋₆alkyl which is unsubstituted or substituted with one or more substituents independently selected from hydroxy, halogen, and amino.~~

*Sub
A5*

25

19. A compound or salt according to Claim 18, wherein:

~~Q is selected from phenyl, pyridyl, pyrimidinyl, pyrazolyl, triazolyl, imidazolyl, pyrrolyl, piperidinyl, and pyrrolidinyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently~~

selected from: halogen, hydroxy, C₁₋₆alkoxy, -CN, amino, mono- and di(C₁₋₆)alkylamino, and C₁₋₆ alkyl which is unsubstituted or substituted with 1 or more substituents chosen from hydroxy, oxo, amino, halogen, C₁₋₆alkoxy, and mono- and di(C₁₋₆)alkylamino; or

5

Q is a group of the formula NR₈R₉ wherein:

*Sub
A5
cont.*
10 R₈ and R₉ are independently hydrogen or C₁₋₆ alkyl which is unsubstituted or substituted with 1 or more substituents chosen from hydroxy, oxo, amino, halogen, and C₁₋₆alkoxy, and mono- and di(C₁₋₆)alkylamino; or

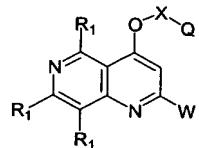
15 R₈, R₉ and the nitrogen to which they are attached form a pyrrolidinyl or piperidinyl ring which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C₁₋₆alkoxy, -CN, amino, mono- and di(C₁₋₆)alkylamino, and C₁₋₆ alkyl which is unsubstituted or substituted with 1 or more substituents chosen from hydroxy, oxo, amino, halogen, C₁₋₆alkoxy, and mono- and di(C₁₋₆)alkylamino; and

20

25 W is phenyl or pyridyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C₁₋₆alkoxy, -nitro, -CN, -SO₂NH₂, -SO₂NHR₂, -SO₂N(C₁₋₆alkyl)₂, amino, -NHC₁₋₆alkyl, -N(C₁₋₆alkyl)₂, -N(C₁₋₆alkyl)CO(C₁₋₆alkyl), -N(C₁₋₆alkyl)CO₂(C₁₋₆alkyl), -CONH₂, -CONH(C₁₋₆alkyl), -CON(C₁₋₆alkyl)₂, -CO₂(C₁₋₆alkyl), -S(C₁₋₆alkyl), -SO(C₁₋₆alkyl), -SO₂(C₁₋₆alkyl), and C₁₋₆alkyl which is unsubstituted or substituted with one or more substituents independently selected from hydroxy, halogen, and amino.

30

20. A compound according to claim 1 of the formula:



21. A compound according to claim 20, wherein X is CH_2 .

5 22. A compound or salt according to claim 21 wherein:

W is phenyl or pyridyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, $\text{C}_{1-6}\text{alkoxy}$, -nitro, -CN, $-\text{SO}_2\text{NH}_2$, $-\text{SO}_2\text{NHR}_2$, $-\text{SO}_2\text{N}(\text{C}_{1-6}\text{alkyl})_2$, amino, $-\text{NHC}_{1-6}\text{alkyl}$, $-\text{N}(\text{C}_{1-6}\text{alkyl})_2$, $-\text{N}(\text{C}_{1-6}\text{alkyl})\text{CO}(\text{C}_{1-6}\text{alkyl})$, $-\text{N}(\text{C}_{1-6}\text{alkyl})\text{CO}_2(\text{C}_{1-6}\text{alkyl})$, $-\text{CONH}_2$, $-\text{CONH}(\text{C}_{1-6}\text{alkyl})$, $-\text{CON}(\text{C}_{1-6}\text{alkyl})_2$, $-\text{CO}_2(\text{C}_{1-6}\text{alkyl})$, $-\text{S}(\text{C}_{1-6}\text{alkyl})$, $-\text{SO}(\text{C}_{1-6}\text{alkyl})$, $-\text{SO}_2(\text{C}_{1-6}\text{alkyl})$, and $\text{C}_{1-6}\text{alkyl}$ optionally substituted with one or more substituents independently selected from hydroxy, halogen, and amino.

15 23. A compound or salt according to Claim 21;

Q is selected from phenyl, pyridyl, pyrimidinyl, pyrazolyl, triazolyl, imidazolyl, pyrrolyl, piperidinyl, and pyrrolidinyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, $\text{C}_{1-6}\text{alkoxy}$, -CN, amino, mono- and di(C_{1-6})alkylamino, and C_{1-6} alkyl which is unsubstituted or substituted with 1 or more substituents chosen from hydroxy, oxo, amino, halogen, $\text{C}_{1-6}\text{alkyl}$, $\text{C}_{1-6}\text{alkoxy}$, and mono- and di(C_{1-6})alkylamino; and

25 W is phenyl or pyridyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, $\text{C}_{1-6}\text{alkoxy}$, -nitro, -CN, $-\text{SO}_2\text{NH}_2$, $-\text{SO}_2\text{NHR}_2$, $-\text{SO}_2\text{N}(\text{C}_{1-6}\text{alkyl})_2$, amino, $-\text{NHC}_{1-6}\text{alkyl}$, $-\text{N}(\text{C}_{1-6}\text{alkyl})_2$, $-\text{N}(\text{C}_{1-6}\text{alkyl})\text{CO}(\text{C}_{1-6}\text{alkyl})$, $-\text{N}(\text{C}_{1-6}\text{alkyl})\text{CO}_2(\text{C}_{1-6}\text{alkyl})$, $-\text{CONH}_2$, $-\text{CONH}(\text{C}_{1-6}\text{alkyl})$, $-\text{CON}(\text{C}_{1-6}\text{alkyl})_2$, $-\text{CO}_2(\text{C}_{1-6}\text{alkyl})$, $-\text{S}(\text{C}_{1-6}\text{alkyl})$,

-SO(C₁₋₆alkyl), -SO₂(C₁₋₆alkyl), and C₁₋₆alkyl which is unsubstituted or substituted with one or more substituents independently selected from hydroxy, halogen, and amino.

5 24. A compound or salt according to Claim 20, wherein X is -CH₂(C=O)-.

10 25. A compound or salt according to Claim 24, wherein: W is phenyl or pyridyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C₁₋₆alkoxy, -nitro, -CN, -SO₂NH₂, -SO₂NHR₂, -SO₂N(C₁₋₆alkyl)₂, amino, -NHC₁₋₆alkyl, -N(C₁₋₆alkyl)₂, -CONH₂, -N(C₁₋₆alkyl)CO(C₁₋₆alkyl), -N(C₁₋₆alkyl)CO₂(C₁₋₆alkyl), -CONH(C₁₋₆alkyl), -CON(C₁₋₆alkyl)₂, -CO₂(C₁₋₆alkyl), -S(C₁₋₆alkyl), -SO(C₁₋₆alkyl), -SO₂(C₁₋₆alkyl), and C₁₋₆alkyl which is unsubstituted or substituted with one or more substituents independently selected from hydroxy, halogen, and amino.

20 26. A compound or salt according to Claim 24, wherein: Q is selected from phenyl, pyridyl, pyrimidinyl, pyrazolyl, triazolyl, imidazolyl, pyrrolyl, piperidinyl, and pyrrolidinyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C₁₋₆alkoxy, -CN, amino, mono- and di(C₁₋₆)alkylamino, and C₁₋₆ alkyl which is unsubstituted or substituted with 1 or more substituents independently chosen from hydroxy, oxo, amino, halogen, and C₁₋₆alkoxy, and mono- and di(C₁₋₆)alkylamino; or

30 Q is a group of the formula NR₈R₉, wherein:

35 R₈ and R₉ are independently hydrogen or C₁₋₆ alkyl which is unsubstituted or substituted with 1 or more substituents independently chosen from hydroxy, oxo, amino, halogen, and C₁₋₆alkoxy, and mono- and di(C₁₋₆)alkylamino; or

R₈, R₉ and the nitrogen to which they are attached form a pyrrolidinyl or piperidinyl ring which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C₁₋₆alkoxy, -CN, amino, mono- and di(C₁₋₆)alkylamino, and C₁₋₆ alkyl which is unsubstituted or substituted with 1 or more substituents independently chosen from hydroxy, oxo, amino, halogen, and C₁₋₆alkoxy, and mono- and di(C₁₋₆)alkylamino;

W is phenyl or pyridyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C₁₋₆alkoxy, -nitro, -CN, -SO₂NH₂, -SO₂NHR₂, -SO₂N(C₁₋₆alkyl)₂, amino, -NHC₁₋₆alkyl, -N(C₁₋₆alkyl)₂, -N(C₁₋₆alkyl)CO(C₁₋₆alkyl), -N(C₁₋₆alkyl)CO₂(C₁₋₆alkyl), -CONH₂, -CONH(C₁₋₆alkyl), -CON(C₁₋₆alkyl)₂, -CO₂(C₁₋₆alkyl), -S(C₁₋₆alkyl), -SO(C₁₋₆alkyl), -SO₂(C₁₋₆alkyl), and C₁₋₆alkyl which is unsubstituted or substituted with one or more substituents independently selected from hydroxy, halogen, and amino.

27. A compound according to Claim 1, which is
5-(4-Fluorophenyl)-7-[(2-pyridyl)methyloxy]-thieno[3,2-b]pyridine.

28. A compound according to Claim 1, which is 5-Phenyl-7-[(3-pyridyl)methyloxy]-thieno[3,2-b]pyridine.

29. A compound according to Claim 1, which is
4-[[2-Phenyl-4-quinolinyl]oxy]acetyl]-[(R)-2-hydroxymethyl]-pyrrolidine.

30. A compound according to Claim 1, which is
N,N-Diethyl-2-[(5-phenylthieno[3,2-b]pyridiyl)oxy]-acetamide.

31. A compound according to Claim 1, which is
N,N-Diethyl-2- [[5-(2-fluoro-phenyl)thieno[3,2-b]pyridiyl]oxy]-
acetamide.

5 32. A compound according to Claim 1, which is
N,N-Diethyl-2- [[5-(4-fluoro-phenyl)thieno[3,2-b]pyridiyl]oxy]-
acetamide.

10 33. A compound according to Claim 1, which is
7- [(4-Pyridyl)methyloxy]) -5-phenylthieno[3,2-b]pyridine.

15 34. A compound according to Claim 1, which is
7- [(3-(1H-1,2,3-triazol-4-yl-methyloxy)] -5-phenylthieno[3,2-
b]pyridine.

15 35. A compound according to Claim 1, which is
7- [(3-(1H-1,2,3-triazol-4-yl-methyloxy)] -2-(4-fluorophenyl)-4-
quinoline.

20 36. A compound according to Claim 1, which is
2- [2-(5-Fluoro-pyridin-2-yl)-quinolin-4-yloxy]-1-(2-
hydroxymethyl-pyrrolidin-1-yl)-ethanone.

25 37. A compound according to Claim 1, which is
1- (2-Hydroxymethyl-pyrrolidin-1-yl)-2-(5-phenyl-thieno[3,2-
b]pyridin-7-yloxy)-ethanone.

30 38. A compound according to Claim 1, which is
4- (1-Methyl-1H-[1,2,3]triazol-4-ylmethoxy)-2-phenyl-
quinoline.

39. A compound according to Claim 1, which is
2- [2-(5-Fluoro-pyridin-2-yl)-quinolin-4-yloxy]-1-(2-
hydroxymethyl-pyrrolidin-1-yl)-ethanone.

D00020247 D00020248

40. A compound according to Claim 1, which is
7-(1-Methyl-1H-[1,2,3]triazol-4-ylmethoxy)-5-phenyl-thieno[3,2-b]pyridine.

5

41. A compound according to Claim 1, which is
2-Phenyl-4-(pyridin-3-ylmethoxy)-[1,6]naphthyridine
2-[2-(4-fluoro-phenyl)-[1,6]naphthyridin-4-yloxy]-1-(2-hydroxymethyl-pyrrolidin-1-yl)-ethanone.

10

42. A compound according to Claim 1, which is
2-[2-(4-fluoro-phenyl)-[1,6]naphthyridin-4-yloxy]-1-pyrrolidin-1-yl-ethanone.

15

43. A compound according to Claim 1, which is
2-(2-Phenyl-[1,6]naphthyridin-4-yloxy)-1-pyrrolidin-1-yl-ethanone.

20

44. A compound according to Claim 1, which is
4-(1-Methyl-1H-[1,2,3]triazol-4-ylmethoxy)-2-(4-fluoro-pyrid-2-yl)-quinoline.

25

45. A compound according to Claim 1, which is
7-(1-Methyl-1H-[1,2,3]triazol-4-ylmethoxy)-5-pyrid-2-yl-thieno[3,2-b]pyridine.

30

46. A compound according to Claim 1, which is
N,N-Diethyl-2-[5-(6-fluoro-pyridin-2-yl)-thieno[3,2-b]pyridin-7-yloxy]-acetamide.

47. A compound according to Claim 1, which is

N,N-Diethyl-2-[5-(4-fluoro-pyridin-2-yl)-thieno[3,2-b]pyridin-7-yloxy]-acetamide.

48. A compound according to Claim 1, which is 5-(4-Fluoro-pyridin-2-yl)-7-(pyridin-4-ylmethoxy)-thieno[3,2-b]pyridine.

49. A compound according to Claim 1, which is
7-(1H-[1,2,3]triazol-4-ylmethoxy)-5-(4-fluoro-pyrid-2-yl)-
10 thieno[3,2-b]pyridine.

50. A compound according to Claim 1, which is
N,N-Diethyl-2-(5-pyridin-2-yl)-thieno[3,2-b]pyridin-7-yloxy)-acetamide.

51. A compound according to Claim 1, which is
5-Pyridin-2-yl-7-(pyridin-4-ylmethoxy)-thieno[3,2-b]pyridine.

52. A compound according to Claim 1, which is
2-[2-(5-Fluoro-pyridin-2-yl)-[1,6]naphthyridin-4-yloxy]-1-(2-hydroxymethyl-pyrrolidin-1-yn)-ethanone.

53. A pharmaceutical composition comprising a compound or salt according to Claim 1 combined with at least one pharmaceutically acceptable carrier or excipient.

54. A method for altering the signal-transducing activity
of GABA_A receptors, said method comprising contacting cells
expressing such receptors with a solution comprising a compound
or salt according to Claim 1 at a concentration sufficient to
detectably alter the electrophysiology of the cell, wherein a
detectable alteration of the electrophysiology of the cell

indicates an alteration of the signal-transducing activity of GABA_A receptors.

5 55. A method for altering the signal-transducing activity of GABA_A receptors, said method comprising contacting cells expressing such receptors with a solution comprising a compound or salt according to Claim 1 at a concentration sufficient to detectably alter the chloride conductance in vitro of cell expressing GABA_A receptors.

10

Sub A7 >
15 56. A method according to Claim 40 wherein the detectable alteration of the electrophysiology of the cell is a change in the chloride ion conductance of the cell.

20 57. The method of Claim 41 wherein the cell is recombinantly expressing a heterologous GABA_A receptor and the alteration of the electrophysiology of the cell is detected by intracellular recording or patch clamp recording.

25

58. The method of Claim 41 wherein the cell is a neuronal cell that is contacted in vivo in an animal, the solution is a body fluid, and the alteration in the electrophysiology of the cell is detected as a reproducible change in the animal's behavior.

25

59. The method of Claim 43 wherein the animal is a human, the cell is a brain cell, and the fluid is cerebrospinal fluid.

30

60. A method for altering the signal-transducing activity of GABA_A receptors, the method comprising exposing cells expressing GABA_A receptors to a compound or salt according to Claim 1 at a concentration sufficient to inhibit RO15-1788 binding in vitro to cells expressing a human GABA_A receptor.

00000000000000000000000000000000

61. A method for the treatment of anxiety, depression, a sleep disorder, or Alzheimer's dementia comprising administering a therapeutically effective amount of a compound or salt of Claim 1 to a patient in need thereof.

5

62. A method for demonstrating the presence of GABA_A receptors in cell or tissue samples, said method comprising:

preparing a plurality of matched cell or tissue samples,

preparing at least one control sample by contacting (under conditions that permit binding of RO15-1788 to GABA_A receptors within cell and tissue samples) at least one of the matched cell or tissue samples (that has not previously been contacted with any compound or salt of Claim 1) with a control solution comprising a detectably-labeled preparation of a selected compound or salt of Claim 1 at a first measured molar concentration, said control solution further comprising an unlabelled preparation of the selected compound or salt at a second measured molar concentration, which second measured concentration is greater than said first measured concentration,

preparing at least one experimental sample by contacting (under conditions that permit binding of RO15-1788 to GABA_A receptors within cell and tissue samples) at least one of the matched cell or tissue samples (that has not previously been contacted with any compound or salt of Claim 1) with an experimental solution comprising the detectably-labeled preparation of the selected compound or salt at the first measured molar concentration, said experimental solution not further comprising an unlabelled preparation of any compound or salt of any one of Claims 1 at a concentration greater than or equal to said first measured concentration;

washing the at least one control sample to remove unbound selected compound or salt to produce at least one washed control sample;

washing the at least one experimental sample to remove unbound selected compound or salt to produce at least one washed experimental sample;

5 measuring the amount of detectable label of any remaining bound detectably-labeled selected compound or salt in the at least one washed control sample;

measuring the amount detectable label of any remaining bound detectably-labeled selected compound or salt in the at least one washed experimental sample;

10 comparing the amount of detectable label measured in each of the at least one washed experimental sample to the amount of detectable label measured in each of the at least one washed control sample

15 wherein, a comparison that indicates the detection of a greater amount of detectable label in the at least one washed experimental sample than is detected in any of the at least one washed control samples demonstrates the presence of GABA_A receptors in that experimental sample.

20 63. The method of Claim 48 in which the cell or tissue sample is a tissue section.

25 64. The method of Claim 48 in which the detectable label is a radioactive label or a directly or indirectly luminescent label.

30 65. The method of Claim 48 in which each cell or tissue sample is a tissue section, the detectable label is a radioactive label or a directly or indirectly luminescent label, and the detectable label is detected autoradiographically to generate an autoradiogram for each of the at least one samples.

35 66. The method of Claim 48 in which each measurement of the amount of detectable label in a sample is carried out by

~~v~~iewing the autoradiograms and the comparison is a comparison of the exposure density of the autoradiograms.

67. A package comprising a pharmaceutical composition of
5 claim 36 in a container and further comprising indicia comprising at least one of:

instructions for using the composition to treat a patient suffering from an anxiety disorder, or

10 instructions for using the composition to treat a patient suffering from depression, or

instructions for using the composition to treat a patient suffering from a sleeping disorder.

Sw
A8
P
COM.
15
Congressional Record

68. A package comprising a pharmaceutical composition of
15 claim 36 in a container and further comprising indicia comprising at least one of: instructions for using the composition to treat a patient suffering from Alzheimer's dementia or instructions for using the composition to enhance cognition in a patient.

20 69. A package comprising a pharmaceutical composition of
claim 37 in a container and further comprising indicia comprising at least one of:

25 instructions for using the composition to treat a patient suffering from an anxiety disorder, or

instructions for using the composition to treat a patient suffering from depression, or

instructions for using the composition to treat a patient suffering from a sleeping disorder.

30 70. A package comprising a pharmaceutical composition of
claim 37 in a container and further comprising indicia comprising at least one of: instructions for using the composition to treat a patient suffering from Alzheimer's

*Sub
A8
cont.*

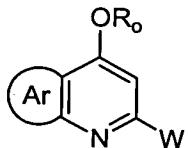
dementia or instructions for using the composition to enhance cognition in a patient.

71. The use of a compound or salt according to Claim 1 for the manufacture of a medicament.

72. The use of a compound or salt according to Claim 1 for the manufacture of a medicament.

10 73. The use of a compound or salt according to Claim 1 for the treatment of anxiety, depression, a sleep disorder, or Alzheimer's dementia.

74. A compound of the formula:

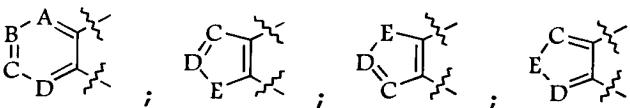


15 where

R_o is hydrogen, C₁-C₆ alkyl, C₁-C₆ alkoxy(C₁-C₆)alkyl, C₁-C₆alkylthio(C₁-C₆)alkyl, allyl, phenacyl, cyclohexyl, benzyl, o-nitrobenzyl, 9-anthrylmethyl, 4-picollyl, t-butylidimethylsilyl, C₁-C₆ alkoxy(C₁-C₆)alkoxy(C₁-C₆)alkyl, or arylacyl, arylpivaloyl, arylbenzoyl, aryl 9-fluorenecarbonyl, arylmethyloxycarbonyl, C₁-C₆ acyl; aryl 2,2,2-trichloroethoxycarbonyl, aryl vinyl oxycarbonyl, aryl benzyloxy carbonyl, aryl methanesulfonyl; and



25 represents:



wherein:

A, B, C, and D are independently nitrogen or CR₁, and E represents oxygen, sulfur or NR₂,

30 wherein

when Ar is a 6-membered ring, 1 or 2 of A, B, C, and D are nitrogen; and

when Ar is a 5-membered ring, C and D are both CR₁ and E is nitrogen, sulfur, or NR₂,

5 where

R₁, at each occurrence, is independently selected from the group consisting of hydrogen, halogen, cyano, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, C₁₋₆ alkyl, amino, mono and di(C₁₋₆)alkylamino, and C₁₋₆ alkoxy; and

10 R₂ is selected from the group consisting of hydrogen, halogen, cyano, halo(C_{1-C₆})alkyl, halo(C_{1-C₆})alkoxy, hydroxy, C₁₋₆ alkyl, amino, and mono or di(C_{1-C₆})alkylamino; and

15 W is selected from the group consisting of aryl, heteroaryl, and heterocycloalkyl, each of which is unsubstituted or substituted with one or more R₃;

20 R₃ is selected from the group consisting of hydrogen, halogen, hydroxy, -OR₆, -NO₂, -CN, -SO₂NH₂, -SO₂NHR₆, -SO₂N(R₆)₂, amino, -NHR₆, -N(R₆)₂, -N(R₆)CO(R₆), -N(R₆)CO₂(R₆), -CONH₂, -CONH(R₆), -CON(R₆)₂, -CO₂(R₆), -S(R₆), -SO(R₆), -SO₂(R₆), and R₇, wherein

25 R₆, at each occurrence, is independently selected from the group consisting of C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkenyl, and C₅₋₉ cycloalkynyl, each of which is unsubstituted or substituted with one or more substituents selected from the group consisting of hydroxy, oxo, halogen, amino, C₁₋₈ alkoxy, and C₁₋₈ alkyl,

30 R₇ at each occurrence is independently selected from the group consisting of C₁₋₈ alkyl, C₁₋₈ alkenyl, C₁₋₈ alkynyl, C₃₋₈ cycloalkyl, C₃₋₈ cycloalkenyl, and C₅₋₉ cycloalkynyl, each of which is unsubstituted or substituted with one or more

35

5
10

substituents selected from the group consisting of hydroxy, oxo, halogen, -OR₆, C₁₋₆alkyl, -NO₂, -CN, -SO₂NH₂, -SO₂NHR₆, -SO₂N(R₆)₂, amino, -NHR₆, -N(R₆)₂, -N(R₆)CO(R₆), -N(R₆)CO₂(R₆), -CONH₂, -CONH(R₆), -CON(R₆)₂, -CO₂H, -CO₂(R₆), -S(R₆), -SO(R₆), -SO₂(R₆), and NR_aR_b, wherein each NR_aR_b independently forms a monocyclic or bicyclic ring each of which may contain one or more double bonds, or one or more of oxo, O, S, SO, SO₂, NH, or N(R₂), wherein R₂ is defined above and independently selected at each occurrence.

15
20

75. A compound according to claim 74, wherein R_o is hydrogen, C_{1-C₆} alkyl, methoxymethyl, methylthiomethyl, allyl, phenacyl, cyclohexyl, benzyl, o-nitrobenzyl, 9-anthrylmethyl, 4-picoly, t-butyldimethylsilyl, and 2-methoxyethoxymethyl.

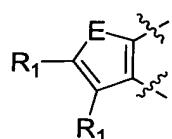
25
30

76. A compound according to claim 74, wherein R_o is hydrogen.

77. A compound according to claim 74, wherein Ar is a 6-membered ring where B is nitrogen and A, C, and D are independently CR₁.

78. A compound according to claim 74, wherein Ar is a 6-membered ring where A is nitrogen and B, C, and D independently represent CR₁.

79. A compound according to claim 74, wherein Ar represents



where E is NR₂ or sulfur.

80. A compound according to claim 79, wherein E is sulfur.

5 81. A compound according to claim 80, wherein W is pyridyl or phenyl, each of which is optionally substituted with from 1 to 3 groups independently selected from halogen, hydroxy, C₁-C₃ alkyl, and C₁-C₃ alkoxy.

10 82. A compound according to claim 74, which is
5-(4-Fluorophenyl)-thieno[3,2-b]pyridin-7-ol;
6-(4-Fluorophenyl)-thieno[2,3-b]pyridin-4-ol;
6-(4-Fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-4-ol;
5-(6-Fluoro-pyridin-3-yl)-thieno[3,2-b]pyridin-7-ol;
15 5-(5-fluoro-pyridin-2-yl)-thieno[3,2-b]pyridin-7-yl
butyrate;
2-(4-fluoro-phenyl)-quinolin-4-yl acetate;
2-Pyridin-3-yl-quinolin-4-ol;
5-Phenyl-thieno[3,2-b]pyridin-7-ol;
20 2-Phenyl-quinolin-4-ol;
5-(2-Fluoro-phenyl)-thieno[3,2-b]pyridin-7-ol;
2-(4-Fluoro-phenyl)-quinolin-4-ol;
2-(5-Fluoro-pyridin-2-yl)-quinolin-4-ol;
2-(5-Fluoro-pyridin-2-yl)-[1,6]naphthyridin-4-ol;
25 2-(4-Fluoro-phenyl)-[1,6]naphthyridin-4-ol;
2-Phenyl-[1,6]naphthyridin-4-ol;
2-Pyridin-2-yl-[1,6]naphthyridin-4-ol;
5-(3-Fluoro-pyridin-2-yl)-thieno[3,2-b]pyridin-7-ol;
5-(5-Fluoro-pyridin-2-yl)-thieno[3,2-b]pyridin-7-ol;
30 6-Phenyl-thieno[2,3-b]pyridin-4-ol;
2-(3-Fluoro-pyridin-2-yl)-[1,6]naphthyridin-4-ol;
5-Pyridin-2-yl-thieno[3,2-b]pyridin-7-ol;
2-(5-Chloro-pyridin-2-yl)-quinolin-4-ol;

2-(5-Bromo-pyridin-2-yl)-[1,6]naphthyridin-4-ol;
2-(4-Chloro-phenyl)-[1,6]naphthyridin-4-ol;
5-(3-Chloro-2-methyl-pyridin-2-yl)-thieno[3,2-b]pyridin-7-
ol; and
5-(5-Chloro-2-ethyl-pyridin-2-yl)-thieno[3,2-b]pyridin-7-
ol.

10

15

20

25